Effect of TGF-beta 1 antisense oligodeoxynucleotide on renal function in chronic renal failure rats

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Abstract:

Aim: The aim of the present study was to investigate the effectiveness of transforming growth factor (TGF)-beta 1 antisense oligodeoxynucleotides (ODN) in ameliorating deteriorated kidney function in rats with puromycin-induced chronic renal failure (CRF). Methods: Saline, puromycin, puromycin+TGF-beta 1 antisense ODN or puromycin+scrambled ODN were administered to unilaterally nephrectomized rats. Renal hemodynamic and excretory measurements were taken in the anaesthetized rats that had undergone surgical procedure. Results: It was observed that in the CRF rats, there was a marked reduction in the renal blood flow (RBF), glomerular filtration rate (GFR), severe proteinuria, and almost 6-fold increased fractional excretion of sodium (FE Na+) as compared to that in the control rats (all $P < 0.05$). It was further observed that in the CRF rats, the treatment with TGF-beta 1 antisense, but not scrambled ODN, markedly attenuated the reduction of RBF, GFR, and proteinuria and markedly prevented the increase of the FE Na+ (all $P < 0.05$). In addition, the renal hypertrophy in the CRF group ($P < 0.05$ vs non-renal failure control) was markedly attenuated after treatment with TGF-1 antisense ODN ($P < 0.05$). Focal segmental glomerulosclerosis was evident only in the untreated and scrambled ODN-treated CRF groups. An interesting observation of this study was that in the CRF rats, although there was marked attenuating and preventive effects of the TGF-beta 1 antisense ODN on the deteriorated renal functions, the antisense treatment did not cause any marked change in the renal expression of TGF-beta 1 at the protein level. Conclusion: Collectively, the data obtained suggests that TGF-beta 1 antisense ODN possesses beneficial effects in puromycin-induced chronic renal failure and that the deterioration in morphology and impaired renal function in this pathological state is in part dependent upon the action of TGF-beta 1 within the kidney.

Keywords:

chronic renal failure, transforming growth factor-β1, antisense oligodeoxynucleotides, renal function

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